DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

T1936M HFI-35

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

JUL 22 1998

OVERNIGHT MAIL

Ref. No. : 98-HFD-340-0701

James A. Lane, J.D.
Director
Kaiser Foundation Research Institute
1800 Harrison Street
Oakland, California 94612

Dear Mr. Lane:

On February 9-18 and March 2-3, 1998, Marie K. Kinkade and Cynthia L. Evitt, investigators with the San Francisco District Office of the Food and Drug Administration (FDA), conducted an inspection of the Kaiser Foundation Hospitals Northern California Institutional Review Board (IRB). The purpose of this inspection was to determine whether your procedures for the protection of human subjects complied with Title 21, Code of Federal Regulations (CFR), Parts 50 and 56. These regulations apply to clinical studies of products regulated by FDA.

At the conclusion of the inspection, Ms. Kinkade issued a Form FDA 483 [enclosure #1] to Nancy R. King, M.Ed., M.P.A., Administrative Manager, Kaiser Foundation Research Institute, which described the deviations from requirements specified under 21 CFR Part 50 and 56 that she had identified during the inspection.

The Agency has reviewed the documents and records relating to the IRB's responsibilities for the protection of subjects of research contained in Ms. Kinkade's and Ms. Evitt's inspection report and the objectionable conditions and practices listed in the current Form FDA 483. The evidence shows that the IRB has failed to adhere to pertinent federal regulations as contained in 21 CFR 50, 56 and 312. The Agency's findings represent significant violations of the Federal Food, Drug, and Cosmetic Act.

Summary of IRB Functions and Operations Violations [21 CFR 56.108(a)(1), 56.109(f), 312.35, 312.53 and 312.61]:

1. The IRB has failed to assure that a licensed practitioner who receives an investigational drug for treatment use under a treatment protocol, as directed by the IRB procedure entitled "Regional Policy and Procedure 63G, Investigational Drugs and Devices" [Procedure 63G], is an "investigator" under the protocol and meets all applicable investigator responsibilities under 21 CFR Parts 50, 56 and 312 [see item #3

in Form FDA 483]. We note that the agency rescinded a December 2, 1994 suspension of the use of Procedure 63G by your IRB on January 25, 1996 [enclosure #2] based upon your IRB's assurance that the use of Procedure 63G was to be conducted in compliance with FDA regulations governing research [enclosure #3]. However, the inspection report shows that Procedure 63G has continued to be used by your IRB to permit physicians who are unqualified investigators under FDA regulations to receive and dispense investigational drugs for treatment use under treatment protocols.

2. The inspection report shows that the IRB has failed to conduct continuing review of ongoing research at intervals not less than once per year [see item #4 in Form FDA 483].

Summary of IRB Records Violation [21 CFR 56.115(a)(1)]

3. The inspection report shows that the IRB has failed to maintain copies of study protocols reviewed by the IRB [see item #1 in Form FDA 483].

Summary of Informed Consent Violations [21 CFR 50.20, 50.25(a)(1)(2) and (7)]

4. The following comments pertain to the consent forms approved by the IRB for the research studies entitled: [redacted] [Study C] and "[redacted] [Study D] [see item #2 in Form FDA 483].

- The last sentence in the first paragraph on page one of these consent forms states: "Its [drug or device] use is experimental until approved by the Food and Drug Administration" Since this statement anticipates FDA approval of the test article, this statement is unduly influential within the meaning of 21 CFR 50.20.

- The consent forms for Studies A, B and C fail to include a statement regarding the expected duration of the subject's participation and a description of the procedures to be followed, and identification of any procedures that are experimental.

- The consent forms for Studies A, B and C fail to include the number and type of clinical test procedures that are performed during the study. Accordingly, these consent forms fail to include an adequate description of reasonably foreseeable risks or discomforts to the subject.

- These consent forms fail to include a person or office to contact in the event of a research-related injury to the subject. Additionally, Study A also fails to include a

person or office to contact for answers to pertinent questions about the research subjects' rights.

The above cited violations may not be all inclusive of the deficiencies in your IRB operation.

Administrative Restrictions

We have no assurance that your procedures are adequately protecting the rights and welfare of human subjects of research. *For this reason, in accordance with 21 CFR 56.120(b)(1) and (2),*

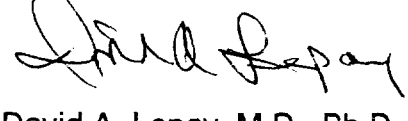
- ***no new studies*** *that are subject to Parts 50 and 56 of the FDA regulations are to be approved by your IRB, and*
- ***no new subjects*** *are to be admitted to ongoing studies that are subject to 21 CFR Parts 50 and 56 until you have received notification from this office that adequate corrections have been made.*

Please inform this office, in writing, within fifteen (15) working days from the date of receipt of this letter, of the actions you have taken or plan to take to bring the procedures of your IRB into compliance with FDA requirements. Please include a copy of any revised documents, such as written procedures, with your response. Any plans of action must include projected completion dates for each action to be accomplished.

If you have any questions, please contact Ms. Mary Jo Zollo at (301) 594-1026, Fax: (301) 594-1204. Your written response should be addressed to:

Mary Jo Zollo, Acting Team Leader
Human Subject Protection Team, (HFD-343)
Division of Scientific Investigations
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Sincerely yours,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

ENCLOSURES
#1 - Form FDA 483
#2 - January 25, 1996 letter from Paul W. Goebel, Jr., FDA to Glenda R. Marlow, Administrative Manager, Kaiser Foundation Research Institute
#3 - December 12, 1995 letter from Glenda R. Marlow, Administrative Manager, Kaiser Foundation Research Institute to Paul W. Goebel, Jr., FDA

cc:
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